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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,300	10/24/2005	Wolfgang Meder	37998-237420	2359

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EXAMINER	
KEMMERER, ELIZABETH	
ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,300	MEDER ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-26* is/are pending in the application.

4a) Of the above claim(s) *14,15,19-24 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13,16-18 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/29/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 11-13, 16-18, and 25, in the reply filed on 09 Jul 2007 is acknowledged.

Claims 14, 15, 19-24, and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 09 July 2007.

Status of Application, Amendments, And/Or Claims

The preliminary amendment of 29 April 2005 has been entered in full. Claims 1-10 are canceled. Claims 14, 15, 19-24, and 26 are withdrawn from consideration as discussed above. Claims 11-13, 16-18, and 25 are under examination.

Specification

The disclosure is objected to because of the following informalities: the specification does not contain appropriate headings as per 37 C.F.R. 1.77(b). Also, the Brief Description of the Drawings fails to refer to parts A and B of Figures 9 and 10. Finally, the Brief Description of the Drawings fails to define the abbreviations for the cell types referred to in Figure 9AB or the abbreviations for skin diseases in Figure 10AB.

Appropriate correction is required.

Claim Objections

Claims 11, 12, and 25 are objected to because of the following informalities: Claims 11 and 12 recite "derivative" in the preamble, which is singular, and then refer to "derivatives" in the body of the claims, which is plural. Claim 25 misspells the word "polypeptide" as "polypeptode" in the second line of the claim. Appropriate correction is required.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16, 17, and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "usual" in claim 16 is a relative term which renders the claim indefinite. The term "usual" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 17 recites a lyophilized form "taken up" with mannitol. It is not clear what is meant by this term. Is the lyophilized form dissolved in a solution with mannitol, or is dry mannitol also present in the lyophilized form?

One alternative in claim 25 recites "the receptor activity triggered by the COM polypeptide ... is greater than the receptor activity triggered by COM", which makes no sense.

35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 11-13 and 25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to COM polypeptides or derivatives, with claim 13 further reciting a GORI-28 receptor. Such polypeptides exist in nature. Natural products do not constitute patentable subject matter under 35 U.S.C. § 101, as they do not show the "hand of man." Amending the claims to specify that the polypeptides are "isolated" or "purified" would be remedial.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 11,12, 16, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by WO9855508A2 (SAGAMI CHEMICAL RESEARCH CENTER; published 10 December 1998).

WO9855508A2 teaches a polypeptide having the amino acid sequence of SEQ ID NO: 1. WO9855508A2 calls this protein "HP10433 rather than "COM" however, the name of the protein is not given weight as long as the structural and functional limitations are met. Note that "having" in claim 11 is interpreted as "comprising." Claim 11 also requires a function wherein the polypeptide activates a GORI-28 receptor. While WO9855508A2 does not disclose this, it is considered an inherent feature of the fully disclosed polypeptide. A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). See pp. 54-55 and SEQ ID NO: 17 of WO9855508A2.

Claim 11 also recites a derivative in the alternative, wherein the derivative has a length of not more than 150 amino acids. Since the derivative is recited in the alternative, WO9855508A2 meets the limitations of the claim even in the full length HP10433 protein of SEQ ID NO: 17. However, it is also noted that WO9855508A2 teaches fragments of the full length protein lacking the N-terminal transmembrane domain at p. 7. Therefore, the shorter derivative is also taught.

Claim 12 recites various derivatives, including glycosylated forms. Such is taught by WO9855508A2 in the sentence bridging pp. 7-8.

Claim 16 is directed to a pharmaceutical composition comprising a COM polypeptide or derivative, optionally in addition to adjuvants and additives. The term "pharmaceutical" is interpreted as an intended use in therapy, and thus a reference disclosing any composition comprising a COM polypeptide, with or without adjuvants or additives, would be considered to e anticipatory, as long as the composition was not inconsistent with use as a pharmaceutical composition. WO9855508A2 teaches such compositions at the bottom of p. 3

Finally, claim 25 is directed to a COM polypeptide or derivative with a confusing functional limitation regarding the degree of receptor activation. (See rejection under 35 U.S.C. § 112, second paragraph, above for a discussion of the confusing limitation). In view of the lack of clarity of the functional limitation, WO9855508A2 also anticipates claim 25.

Claims 11, 13, 16, and 25 are rejected under 35 U.S.C. 102(e) as being anticipated by US 20030096299A1 (Wittamer et al.; effective filing date 09 July 2001).

'299 teaches a polypeptide called TIG2 having (interpreted as "comprising") the amino acid sequence of SEQ ID NO: 1. See SEQ ID NO: 8 and Figure 6. Claim 11 recites a derivative of no more than 150 amino acids; however, since this derivative is recited in the alternative only, '299 fully anticipates the structural requirement of a COM polypeptide "having the amino acid sequence of SEQ ID NO: 1." '299 does not call their polypeptide "COM"; however, the name of a polypeptide is given no patentable weight since it does not affect the structure or function of the polypeptide itself. Finally, '299

does not state that their polypeptide activates a GORI-28 polypeptide; however, this is an inherent feature of the polypeptide since it has the same structure. A compound and its properties are inseparable.

Claim 13 further recites a GORI-28 polypeptide. '299 teaches a polypeptide-receptor complex at paragraphs [0038] and [0114] for example. '299 calls the receptor "ChemR23" rather than GORI-28; however, as stated above, the name of a polypeptide is given no patentable weight since it does not affect the structure or function of the polypeptide itself.

Claim 16 is directed to a pharmaceutical composition comprising a COM polypeptide or derivative, optionally in addition to adjuvants and additives. The term "pharmaceutical" is interpreted as an intended use in therapy, and thus a reference disclosing any composition comprising a COM polypeptide, with or without adjuvants or additives, would be considered to be anticipatory, as long as the composition was not inconsistent with use as a pharmaceutical composition. '299 teaches such compositions at paragraph [0038].

Finally, claim 25 is directed to a COM polypeptide or derivative with a confusing functional limitation regarding the degree of receptor activation. (See rejection under 35 U.S.C. § 112, second paragraph, above for a discussion of the confusing limitation). In view of the lack of clarity of the functional limitation, '299 also anticipates claim 25.

35 U.S.C. § 112, First Paragraph – Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-13, 16-18, and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed invention wherein the recited COM polypeptide comprises SEQ ID NO: 1 and the recited GORI-28 receptor encode by the nucleic acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for the invention as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make an/or use the invention commensurate in scope with these claims.

The claims are directed to COM polypeptides or a derivative thereof having at least 80% sequence identity to the COM polypeptide of SEQ ID NO: 1 while retaining the receptor activation activity. The GORI-28 receptor recited in claim 13 recites no limitations regarding structure or function.

The specification discloses one sequence for human COM (SEQ ID NO: 1) and one sequence to define a GORI-28 receptor (encoded by SEQ ID NO: 2). There is no detailed guidance regarding what sorts of sequence alterations can be tolerated by either molecule without loss of function.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success

are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at

Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Due to the large quantity of experimentation necessary to generate the large number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which recite only broad structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 U.S.C. § 112, First Paragraph – Written Description

Claims 11-13, 16-18, and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As discussed above, the claims define a genus of COM polypeptides or a derivative thereof, as well as a genus of structurally undefined GORI-28 receptor molecules. To provide evidence of possession of a claimed genus, the specification

must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity plus a vague functional requirement for COM derivatives. The GORI-28 receptor is not defined structurally or functionally. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NO: 1 for COM and the polypeptide encoded by SEQ ID NO: 2 for GORI-28, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The

compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 1 and encoded by the nucleic acid sequence of SEQ ID NO: 2, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (571) 272-0874. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D. can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ECK

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